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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/652,292	08/31/2000	Donald W. Bowden	9151-11	4240

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EXAMINER	
BASI, NIRMAL SINGH	
ART UNIT	**PAPER NUMBER**
1646	7

DATE MAILED: 05/07/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.	Applicant(s)
09/652,292	Bowden et al
Examiner	**Art Unit**
Nirmal S. Basi	1646

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on *Feb 12, 2002* .

2a) ☐ This action is **FINAL.** 2b) ☒ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *1-36* is/are pending in the application.

4a) Of the above, claim(s) *10-35* is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *1-9 and 36* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

15) ☒ Notice of References Cited (PTO-892)
16) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
17) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____
18) ☐ Interview Summary (PTO-413) Paper No(s). _____
19) ☐ Notice of Informal Patent Application (PTO-152)
20) ☐ Other:

DETAILED ACTION

1. Response to Restriction requirement filed 2/12/02 (paper number 6) has been entered.

Election/Restriction

2. Applicant's election with traverse of Group II (Claims 1-9 and 36), in Paper No. 7 (7/26/00), is acknowledged. The traversal is on the ground(s) that the polynucleotides of Group II and the inventions of Groups I and III-VII should be examined together because a search of the subject matter of Group II and II-VII would overlap and that such a search and examination would not put a serious burden on the examiner. This is not found persuasive because a search of Groups II would not be co-extensive with groups I and III-VII particularly with regard to the literature search as shown by the different classification of said groups. An examination of the materially different, patentably distinct inventions in a single application would constitute a serious undue burden on the examiner.

The requirement is still deemed proper and is therefore made FINAL.

3. The drawings objected to because each Figure must described separately in the Brief Description of the Drawings. For example, Figure 1 must described as Figures 1A and B in the beginning of the description section of said figure. Similarly Figure 3 must be described as Figures 3A and 3B, Figure 4 as Figures 4A, B and C, or the equivalent, as required by 37 C.F.R. § 1.84 (u)(1).

Appropriate correction is required.

4. ***Sequence Rules Compliance***

This application fails to comply with the sequence rules, 37 CFR 1.821-1.825. Nucleotide and polypeptide sequences must be identified with the corresponding SEQ ID NO. Title 37, Code of Federal Regulations, Section 1.821 states "reference must be made to the sequence by use of the assigned identifier", the identifier being SEQ ID NO. Sequences in Figure 1 and 2 must be identified by their corresponding SEQ ID NO:. Compliance with sequence rules is required.

Claim Rejections - 35 USC § 101

5. 35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter or any new and useful improvement thereof, may obtain a patent therefore, subject to the conditions and requirements of this title.

Claim 36 is rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter.

Claim 36 recites an oligonucleotide but do not recite that it is isolated or purified. The claim as currently recited encompasses these naturally-occurring compounds. Therefore, the compounds as claimed are a product that occurs in nature and does not show the hand of man, and as such is non-statutory subject matter. It is suggested that the claims be amended to recite "an isolated and purified" to overcome this rejection.

Claim Rejection, 35 U.S.C. 112

6. Claims 1-9 and 36 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 is indefinite because "stringent conditions" are not specified. The metes and bounds of the group of sequences that would meet the limitations of the claim depend upon the precise conditions under which hybridizations were performed including wash conditions. Since the hybridization and wash conditions dictate which nucleic acid sequences remain specifically bound to the nucleic acid of SEQ ID NO:1 the metes and bounds of the claims cannot be determined without the disclosure of said conditions,

Claim 36 recites the limitation "oligonucleotide that hybridizes to a nucleic acid according to claim 1" . There is insufficient antecedent basis for this limitation of "oligonucleotide" in the claim.

Claims 2-9 are rejected for depending upon an indefinite base (or intermediate) claim and fail to resolve the issues raised above.

35 U.S.C. § 112, first paragraph

7. Claims 1-9 and 36 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an isolated nucleic acid which has the sequence of SEQ ID NO:1, encoding a polypeptide which comprises the polypeptide disclosed in SEQ ID NO:2, isolated

nucleic acid which encodes the polynucleotide of SEQ ID NO:2 due to degeneracy of the genetic code, specific fragments of the nucleic acid of SEQ ID NO:1 which specifically hybridize to the nucleic acid of SEQ ID NO:1 or which encode fragments of the polypeptide of SEQ ID NO:2 which are of sufficient length to raise antibodies to the polypeptide of SEQ ID NO:2, DNA vector comprising said nucleic acid, host cell stably transfected or transformed with said vector does not reasonably provide enablement for other nucleic acids. The, specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Claims 1-9 and 36 are directed to a nucleic acid encoding a glucose transporter protein selected from the group of consisting of:

a) isolated nucleic acid having the sequence of SEQ ID NO:1

b) isolated nucleic acids that hybridize under stringent conditions to the complement of SEQ ID NO:1

c) degenerate sequences of a) and b) which encode a glucose transporter encoded by isolated nucleic acids a) and b)

Further the claims are directed to DNA vector comprising said nucleic acid, host cell stably transfected or transformed with said vector and nucleic acid that hybridize to oligonucleotide according to claim 1.

The claims encompass nucleic acids encoding variants which may be completely unrelated, structurally and functionally, to the polynucleotide of SEQ ID NO:1 encoding the polypeptides of

SEQ ID NO:2. Further, the claims do not disclose specific hybridization conditions, and therefore do not constitute a meaningful structural limitation. The hybridization conditions dictate the scope of the polynucleotides that will hybridize to a particular nucleic acid molecule. Therefore every nucleic acid will be able to hybridize to the to another nucleic acid under non specific binding conditions.

The claims are similar to single means claims in that claims recite any nucleic acid that hybridizes to or encodes a glucose transporter polypeptide or fragments thereof, but the specification only discloses the nucleic acid molecule of SEQ ID NO:1 encoding the polypeptide of SEQ ID NO:2. MPEP 2164.08(a) defines a single means claim as a claim which covered every conceivable means for achieving the stated purpose when the specification disclosed at most only those means known to the inventor. This type of claim was held to be nonenabling for the scope of the claim in In re Hyatt, 708 F.2d 712, 218 USPQ 195 (Fed. Cir. 1983) because the specification disclosed at most only those means known to the inventor. When claims depend on a recited property (i.e. nucleic acid that hybridizes to or encodes a glucose transporter polypeptide), a fact situation comparable to Hyatt is possible, where the claim covers every conceivable structure (means) for achieving the stated property (result) while the specification discloses at most only those known to the inventor. This appears to be the instant case and the claims are not commensurate in scope with the specification.

While the person of ordinary skill in the art, would, in light of the specification, be able to make and isolate polynucleotides encoding polypeptide fragments of SEQ. ID. NO:2, the scope of

the claims, which encompass any nucleic acid encoding any glucose transporter protein or fragments thereof, is simply not enabled by the disclosure. The disclosure does not teach how to use the numerous nucleic acids which would hybridize to the complement of SEQ ID NO:1 and encode polypeptides lacking the critical feature of the claimed invention.

Instant claim also fails to identify the critical structural feature of the invention required for function. The variants encompassed by the claims identified may not contain many of the features of the protein of SEQ ID NO:2, ie. may classified as glucose transporter protein, but be inactive. The claim also encompasses nucleic acids encoding all possible mutations and deletions of the protein. Many of the oligonucleotide that hybridize to the nucleic acid of SEQ ID NO:1 or to degenerate sequence of SEQ ID NO:1 would also hybridize to other nucleic acids or may not hybridize to the nucleic acid of SEQ ID NO:1. Applicant has not disclosed how to use these oligonucleotides. Although the skilled artisan can produce nucleic acid variants and mutants of SEQ ID NO:1, due to the large amount of experimentation necessary to test variants and mutants within the scope of the claim and to determine how to use variants and mutants which are unrelated to SEQ ID NO:1, inactive, the lack of guidance presented in the specification regarding same, the absence of working examples directed to same, the complex nature of the invention, the state of the prior art in the unpredictability of protein folding, and the breadth of the claims which fail to disclose the critical feature of the invention and structural limitations, undue experimentation would be required of the skilled artisan to make and use the claimed invention in its full scope.

Further instant fact pattern closely resembles that in Ex parte Maizel, 27 USPQ2d 1662 (BPAI 1992). In Ex parte Maizel, the claimed invention was directed to compounds which were defined in terms of function rather than sequence (i.e., "biologically functional equivalents"). The only disclosed compound in both the instant case and in Ex parte Maizel was the full length, naturally occurring protein. The Board found that there was no reasonable correlation between the scope of exclusive right desired by Appellant and the scope of enablement set forth in the patent application. Even though Appellant in Ex parte Maizel urged that the biologically functional equivalents would consist of proteins having amino acid substitutions wherein the substituted amino acids have similar hydrophobicity and charge characteristics such that the substitutions are "conservative" and do not modify the basic functional equivalents of the protein, the Board found that the specification did not support such a definition, and that the claims encompassed an unduly broad number of compounds. Such is the instant situation. Clearly, a single disclosed sequence does not support claims to any nucleic acid hybridizing to same, given the lack of guidance regarding what sequences would hybridize specifically to the polynucleotide of SEQ ID NO: 1, and not other, related sequences. Also many of the oligonucleotides of claim 36 may not be useful as hybridization probes which specifically bind to fragments of the polynucleotide of SEQ ID NO:1, due to degeneracy of the genetic code, or encode, non-functional polypeptides. Applicant has not disclosed how to use the aforementioned polynucleotides. Likewise expression vector , host cells comprising said vector of claimed nucleic acid molecules are not enabled for these reasons given above.

Further, there is no description, however, of the sites at which variability may be tolerated, which amino acids are to be substituted to produce the variants encompassed by the claims. Structural features that could distinguish the compounds in the genus from others are missing from the disclosure. There is no disclosure of the critical technical feature of the invention. Many of the variants, mutants and fragments encompassed by the scope of the claims will be inactive or have activities unrelated to the protein of SEQ ID NO:2. The specification does not teach how to make functional variants and mutants encompassed by the claims or to use inactive variants. The prior art teaches that amino acid substitutions produce unpredictable results in a structurally related protein. Furthermore, neither the specification nor the prior art provide any guidance as to which amino acids could be altered, nor does the specification provide any guidance as to how the skilled artisan could use an inactive variants, mutants. Therefore, it would require undue experimentation to practice this invention as claimed, because the skilled artisan would have no reasonable expectation that variants and mutants encompassed could be used for any purpose. Furthermore, the prior art does not provide compensatory structural or correlative teachings sufficient to enable one of skill to make, isolate, identify and use the claimed variant nucleic acid encoding polypeptides encompassed, without undue experimentation.

Therefore, due to the lack of direction/guidance presented in the specification regarding the production, identification, purification, isolation and characterization of the mutants and variants, encompassed by the claims, the unpredictability of the effects of mutation on the structure and function of proteins (since mutations of SEQ ID NO:1 and 2) are also encompassed by the claim),

and the breadth of the claim which fail to recite specific structural and functional limitations, undue experimentation would be required of the skilled artisan to make or use the claimed invention in its full scope.

8. Claims 1, 2, 3, 6-9 and 36 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The instant specification does not contain a written description of the invention in such full, clear, concise, and exact terms or in sufficient detail that one skilled in the art can reasonably conclude that applicant had possession of the claimed invention at the time of filing.

Claims are directed to a nucleic acid encoding a glucose transporter protein selected from the group of consisting of:

b) isolated nucleic acids that hybridize under stringent conditions to the complement of SEQ ID NO:1

c) degenerate sequences of a) and b) which encode a glucose transporter encoded by isolated nucleic acids a) and b)

The specification discloses an isolated cDNA of SEQ ID NO: 1, encodes a distinct polypeptide of SEQ ID NO. 2. The instant disclosure of one distinct polypeptide does not adequately describe the scope of the claimed genus, which encompasses polynucleotide encoding substantial variety of subgenera including full-length, truncated, fusion molecules, variants thereof

and oligonucleotides which hybridize to the nucleic acid of claim 1 (many of the oligonucleotides will not be capable of hybridizing to SEQ ID NO:1 due to degeneracy of the genetic code requirement in the claim). A description of a genus of polypeptides may be achieved by means of a recitation of a representative number of polypeptides, defined by an amino acid sequence, falling within the scope of the genus or of a recitation of structural and functional features common to members of the genus, which features constitute a substantial portion of the genus. *Regents of the University of California v. Eli Lilly & Co.*, 119 F3d 1559, 1569, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997). The instant specification fails to provide sufficient descriptive information, such as definitive structural and functional features of the claimed genus of polypeptides. There is no description of the conserved regions which are critical to the structure and function of the genus claimed. The fusion polypeptides, fragments and variants encompassed by the claims do not disclose the critical technical feature of the claimed invention or its relationship to function. For example, claimed oligonucleotides and nucleic acids encompassed by the claims may be completely unrelated to the disclosed nucleic acid encoding the polypeptide of SEQ ID NO:2, having functionally and structurally or even be inactive. The critical technical feature encompassed by the fragments and variants must relate to the encompassed polypeptide, structurally and functionally to the disclosed protein of SEQ ID NO:2. The same argument applies to the variants and fusion products encompassed by the other claims being examined. It is not clear what critical technical feature the undisclosed amino acids, or disclosed amino acids in a specific fragment, provide so as to show a written description of the invention in full, clear, concise, and exact terms or in sufficient detail that

one skilled in the art can reasonably conclude that applicant had possession of the claimed invention at the time of filing. The specification proposes to discover other members of the genus by using hybridization techniques. There is no description, however, of the sites at which variability may be tolerated and there is no information regarding the relation of structure to function. Structural features that could distinguish the compounds in the genus from others excluded are missing from the disclosure. Furthermore, the prior art does not provide compensatory structural or correlative teachings sufficient to enable one of skill to isolate and identify the polynucleotides encompassed and no identifying characteristic or property of the encoded polypeptides is provided such that one of skill would be able to predictably identify the encompassed molecules as being identical to those instantly claimed.

The specification further fails to identify and describe the regulatory regions essential to the function of the claimed invention, which are required since the claimed invention currently encompasses the full length, truncated, fusion products and variants thereof. Since the disclosure fails to describe the common attributes or characteristics that identify members of the genus, and because the genus may be highly variant, the disclosure is insufficient to describe the genus. One of skill in the art would reasonably conclude that the disclosure fails to provide a representative number of species to describe and enable the genus as broadly claimed.

An adequate written description of a protein or nucleic acid molecule requires a precise definition, such as by structure, formula, chemical name, and physical properties, not a mere wish or plan for obtaining the claimed chemical invention. Accordingly, an adequate written description

of a polypeptide is more than a mere statement that it is part of the invention and reference to a potential method for isolating it; what is required is a description of the polynucleotide or the encoded protein itself. Accordingly, the specification does not provide a written description of the invention of claims 1-3, 6-9 and 36.

One of skill in the art would reasonably conclude that the disclosure fails to provide a representative number of species to describe, enable and use the genus as broadly claimed. The skilled artisan cannot envision the detailed chemical structure of the encompassed proteins and, therefore, conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it. It is acknowledged that the skill of the artisan in the molecular biology art is high. However, in the current instance, **there is no clear evidence of the critical special technical feature of the claimed nucleic acid or how the critical special technical feature encompassed by the genus claimed relates to function.**

Vas-Cath Inc. V. Mahurkar, 19 USPQ2d 1111, clearly states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" (See page 1117). The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (*See Vas-Cath* at page 1116).

Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 USC 112 is severable from its enablement provision (see page 115).

Adequate written description requires more than a mere statement that it is part of the invention and a reference to a potential method of isolating it. The nucleic acid or polypeptide is itself is required. See *Fiers v. Revel*, 25 USPQ 2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. V. Chugai Pharmaceutical Co. Lts.*, 18 USPQ2d 1016.

Furthermore, In *The Reagents of the University of California v. Eli Lilly* (43 USPQ2d 1398-1412), the court held that a generic statement which defines a genus of nucleic acids by only their functional activity does not provide an adequate written description of the genus. The court indicated that while Applicants are not required to disclose every species encompassed by a genus, the description of a genus is achieved by the recitation of a representative number of DNA molecules, usually defined by a nucleotide sequence, falling within the scope of the claimed genus. At section B(1), the court states that "An adequate written description of a DNA...'requires a precise definition, such as by structure, formula, chemical name, or physical properties', not a mere wish or plan for obtaining the claimed chemical invention".

With the exception of SEQ ID NO:1, the skilled artisan cannot envision the detailed chemical structure of the claimed nucleic acid and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it. The nucleic acid itself is required. See Fiers v.

Revel, 25 USPQ2d 1601, 1606 (CAFC 1993) and Amgen Inc v. Chugai Pharmaceutical Co. Ltd., 18 USPQ2d 1016.

One cannot describe what one has not achieved. See Fiddes v. Baird, 30 USPQ2d 1481, 1483. In Fiddes v. Baird, claims directed to mammalian FGFs were found unpatentable due to lack of written description for the broad class.

Therefore, only the polynucleotide of SEQ ID NO:1 encoding the polypeptide of SEQ ID NO:2, specific fragments of SEQ ID NO:1, but not the full breadth of the claim meets the written description provision of 35 U.S.C. 112, first paragraph. Applicant is reminded that Vas-Cath makes clear that the written description provision of 35 USC 112 is severable from its enablement provision. (See page 1115).

Claim Rejections, 35 U.S.C. 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

10. Claims 1,2,36 rejected under 35 U.S.C. 102(b) as being anticipated by Marra et al (Ref A). Marra discloses a mouse nucleic acid capable of hybridizing to the polynucleotide of SEQ ID NO:1. Marra discloses a nucleic acid (EST Database, Locus AI042706, Accession number AI042706),a cDNA clone with 12.5% Query match and 99.5% identity to SEQ ID NO:1 of instant Application. The clone of Marra is inherently an oligonucleotide that hybridizes to the nucleic acid of SEQ ID

NO:1. The nucleic acid (oligonucleotide) disclosed by Marra is inherently a glucose transporter because the post filing art of Ramsay (Ref 2) discloses the Sequence of the cDNA clone of Marra et al is contained in the glucose transporter of clone RP1-28H20 (Locus HS28H20, GenEmbl database, Accession number AL031055). The disclosure of Marra meets the requirements of an isolated nucleic acid or oligonucleotide that hybridizes to the complement of the sequence of SEQ ID NO:1, absent evidence to the contrary.

No claim is allowed.

Advisory Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Nirmal Basi whose telephone number is (703) 308-9435. The examiner can normally be reached on Monday-Friday from 9:00 to 5:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne Eyler, can be reached on (703) 308-6564. The fax phone number for this Group is (703) 308-0294.

Official papers filed by fax should be directed to (703) 308-4242. Faxed draft or informal communications with the examiner should be directed to (703) 308-0294.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Nirmal S. Basi
Art Unit 1646
May 6, 2002

Michael D. Pak

MICHAEL PAK
PRIMARY EXAMINER